



Docket No. 50634-BA/JPW/AJM/JCS

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Eric Rose et al.  
Serial No. : 10/646,493  
Filed : August 21, 2003  
For : METHODS FOR INHIBITING THROMBOSIS IN A PATIENT  
WHOSE BLOOD IS SUBJECTED TO EXTRACORPOREAL  
CIRCULATION

1185 Avenue of the Americas  
New York, New York 10036  
November 19, 2003

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

INFORMATION DISCLOSURE STATEMENT

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the following documents, which are listed on Form PTO-1449 and are also listed below. Copies of documents 1-14 were previously submitted in connection with copending U.S. Serial No. 09/053,872, filed April 1, 1998, a continuation-in-part of U.S. Serial No. 08/648,561, now U.S. Patent 5,839,443, issued November 24, 1998. The documents listed herebelow as items 1-16 are again listed on Form PTO-1449 which is attached hereto as **Exhibit 1**.

1. Bazan, J.F., "Big rigs in blood coagulation," Nature 380: 21-23, 03/1996;
2. Benedict, C.R. et al., "Active site-blocked factor IXa

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- prevents intravascular thrombus formation in the coronary vasculature without inhibiting extravascular coagulation in a canine thrombosis model," J. Clin. Invest., 88: 1760-1765, 1991;
3. Benedict, C.R. et al., "Endothelial-Dependent Procoagulant and Anticoagulant Mechanisms," Texas Heart Institute Journal, 21: 86-90, 1994;
  4. Berntorp, E., "Biochemical and in vivo properties of high purity factor IX concentrates," Thrombosis and Haemostasis 70(5): 768-773, 11/1993;
  5. Freedman, S.J. et al., "Structure of the metal-free  $\gamma$ -carboxyglutamate acid-rich membrane binding region of factor IX by two-dimensional NMR spectroscopy," J. Biol. Chem., 270(14): 7980-7987, 04/1995;
  6. Furie, B.C. and Furie, B., "Biosynthesis of factor IX: implications for gene therapy," Thrombosis and Haemostasis, 74(1): 274-277 (1995);
  7. Iberti, T.J. et al., "Abnormal coagulation profile in brain tumor patients during surgery," Neurosurgery, 34(3): 389-395, 03/1994;
  8. Kirchhofer, et al., "Active site-blocked factors VIIa and IXa differentially inhibit fibrin formation in a human ex vivo

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- thrombosis model," Arterioscler. Thromb. Vasc. Biol., 15: 1098-1106 (1995);
9. Kuwabara, K. et al., "Calreticulin, an antithrombotic agent which binds to vitamin K-dependent coagulation factors, stimulates endothelial nitric oxide production, and limits thrombosis in canine coronary arteries," J. Biol. Chem., 270(14): 8179-8187, 04/1995;
  10. Miyata, T. et al., "Factor IX Bm Kiryu: a Val-313-to-Asp substitution in the catalytic domain results in loss of function due to a conformational change of the surface loop: evidence obtained by chimeric modeling," Brit. J. Of Haematol., 88(1): 156-165, 09/1994;
  11. Santagostino, E. et al., "Markers of hyper coagulability in patients with hemophilia B given repeated, large doses of factor IX concentrates during and after surgery," Thrombosis and Haemostasis, 71(6): 737-40, 06/1994;
  12. Wacey, A.I. et al., "Determinants of the factor IX mutational spectrum in hemophilia B: an analysis of missense mutations using a multi-domain molecular model of the activated protein," Hum. Genet., 94(6): 594-609, 12/1994;
  13. Warriar, I. et al., "Safety of high doses of a monoclonal antibody-purified factor IX concentrate, Am. J. Of Hematol., 49(1): 92-94, 05/1995;

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14. Wong, A.G. et al., "Relative efficacy of active site-blocked factors IXa Xa in a model of venous thrombosis," Supplement I Circulation, Abstract # 3293 p. I-686, Vol. 92, No. 8. 10/1995;
15. Rose, E. et al., U.S. Serial No. 09/053,872, filed April 1, 1998 (**Exhibit 2**); and
16. Rose, E. et al., U.S. Patent No. 5,839,443, issued November 24, 1998 (**Exhibit 3**).

Applicants request that the Examiner review the references and make them of record in the subject application.

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No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. If any such fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

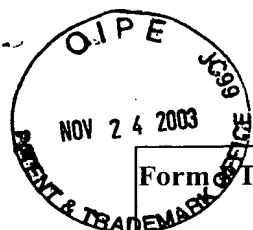
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## U.S. PATENT DOCUMENTS

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
	US 5,839,443	Nov. 24, 1998	Eric Rose, et al.			
	US 09/053,872		Eric Rose, et al.			April 1, 1998

## FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Class	Subclass	Translation	
					Yes	No

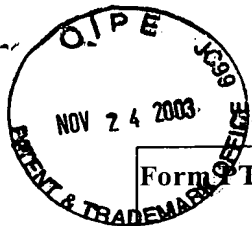
## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Bazan, J.F., "Big rigs in blood coagulation," <u>Nature</u> 380: 21-23, 03/1996
	Benedict, C.R. et al., "Active site-blocked factor IXa prevents intravascular thrombus formation in the coronary vasculature without inhibiting extravascular coagulation in a canine thrombosis model," <u>J. Clin. Invest.</u> , 88: 1760-1765, 1991
	Benedict, C.R. et al., "Endothelial-Dependent Procoagulant and Anticoagulant Mechanisms," <u>Texas Heart Institute Journal</u> , 21: 86-90, 1994
	Berntorp, E., "Biochemical and in vivo properties of high purity factor IX concentrates," <u>Thrombosis and Haemostasis</u> 70(5): 768-773, 11/1993
	Freedman, S.J. et al., "Structure of the metal-free $\gamma$ -carboxyglutamate acid-rich membrane binding region of factor IX by two-dimensional NMR spectroscopy," <u>J. Biol. Chem.</u> , 270(14): 7980-7987, 04/1995
	Furie, B.C. and Furie, B., "Biosynthesis of factor IX: implications for gene therapy," <u>Thrombosis and Haemostasis</u> , 74(1): 274-277 (1995)
	Iberti, T.J. et al., "Abnormal coagulation profile in brain tumor patients during surgery," <u>Neurosurgery</u> , 34(3): 389-395, 03/1994
	Kirchhofer, et al., "Active site-blocked factors VIIa and IXa differentially inhibit fibrin formation in a human ex vivo thrombosis model," <u>Arterioscler. Thromb. Vasc. Biol.</u> , 15: 1098-1106 (1995)

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## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Kuwabara, K. et al., "Calreticulin, an antithrombotic agent which binds to vitamin K-dependent coagulation factors, stimulates endothelial nitric oxide production, and limits thrombosis in canine coronary arteries," <u>J. Biol. Chem.</u> , 270(14): 8179-8187, 04/1995
	Miyata, T. et al., "Factor IX Bm Kiryu: a Val-313-to-Asp substitution in the catalytic domain results in loss of function due to a conformational change of the surface loop: evidence obtained by chimeric modeling," <u>Brit. J. Of Haematol.</u> , 88(1): 156-165, 09/1994
	Santagostino, E. et al., "Markers of hyper coagulability in patients with hemophilia B given repeated, large doses of factor IX concentrates during and after surgery," <u>Thrombosis and Haemostasis</u> , 71(6): 737-40, 06/1994
	Wacey, A.I. et al., "Determinants of the factor IX mutational spectrum in hemophilia B: an analysis of missense mutations using a multi-domain molecular model of the activated protein," <u>Hum. Genet.</u> , 94(6): 594-609, 12/1994
	Warrier, I. et al., "Safety of high doses of a monoclonal antibody-purified factor IX concentrate, <u>Am. J. Of Hematol.</u> , 49(1): 92-94, 05/1995
	Wong, A.G. et al., "Relative efficacy of active site-blocked factors IXa Xa in a model of venous thrombosis," <u>Supplement I Circulation</u> , Abstract # 3293 p. I-686, Vol. 92, No. 8. 10/1995

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